

GLUCOKINASE ACTIVATION BY THE APOPTOTIC PROTEIN BAD

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As a pro-apoptotic member of the Bcl-2 family, BAD neutralizes anti-apoptotic proteins upon cell stress to initiate the apoptotic pathway. BAD may also play a role in glucose homeostasis by forming a complex with glucokinase in hepatic and pancreatic beta cells. Glucokinase is a monomeric enzyme that catalyzes the ATP-dependent phosphorylation of glucose, the rate-limiting step of glycolysis. BAD knockouts result in loss of formation of this complex and blunted glucose-stimulated insulin secretion as well as other glucokinase-related functions. Phosphorylation of BAD is known to block its apoptotic activity and may play a role in stimulating glucokinase activity. We will discuss the implications of the BAD-glucokinase complex formation on glucokinase activity, as well as the role of BAD phosphorylation on the formation and activation of this complex. Our results demonstrate that addition of BAD increases the rate of glucose phosphorylation nearly two-fold over glucokinase alone.